AMENDMENTS

Brackets to signify a deletion are in bold to differentiate them from non-bolded brackets that are to remain as proper text of the specification.

In the Specification:

Please delete Figures 11-16 and insert therefor the formal drawings Figures 11-16, submitted with this application.

At column 2, line 63, through column 3, line 17, please amend the paragraph as follows:

--Ischemia and hypoxia are both conditions that deprive tissue of oxygen, leading to anaerobic metabolism and the accumulation of the metabolic coenzyme NADH. The coenzyme NADH is a fluorescent molecule. Therefore, ischemia and hypoxia can be indirectly detected using LIF techniques by sensing increased concentrations of NADH and interpreting its elevation as a sign of oxygen deficiency. A common indicator of oxygen deficiency is the ratio between the LIF intensity at wavelengths associated with the peak fluorescence emission of NADH, collagen and elastin. However, such methods have not been practically applied for the detection of ischemia because of several complications. First, these methods cannot determine whether the elevated NADH concentration is caused by ischemia, hypoxia or hypermetabolism. Second, scarred or fibrosed tissue would be detected as normal because of their low NADH concentration. Finally, the indicator ratios are calculated by normalizing the intensity of NADH peak fluorescence by that of collagen or elastin. Although the fluorescence of the structural proteins elastin and collagen does not vary with tissue oxygenation, their fluorescence **[**vary**]** varies with the site of measurement.--.

At column 5, lines 6-9, please amend the paragraph as follows:

A2 FIGS. 9(*a*)-(*c*) are partial perspective views of three LIFAS probes having waveguides arranged in different geometrical configurations adapted for different applications (top row is an elevation view; middle row is a side view; bottom row is a bottom view);

At column 9, lines 47-64, please amend the paragraph as follows:

A3 In addition, the signals **224***a* and **225***a* will also exhibit wavelength-dependent modulations caused by the instrumental effects. The wavelength-dependent modulations due to the instrumental effects can be determined and, in turn, compensated for by conducting a calibration of the LIFAS system **210**. System calibration can be performed using light from a standard lamp (Quartz Halogen Lamp, Model No. 63358, Oriel Instruments, Stratford, Conn.) having a predetermined continuous spectrum to measure the wavelength-dependent instrumental effects of the LIFAS system **210**. Once these instrumental effects are known, the processor **223** can be adapted to correct the measured intensities $I_{c1}(\lambda)$ and $I_{c2}(\lambda)$ for modulations caused by the wavelength-dependent instrumental effects. The corrected intensities $I_{c1}(\lambda)^c$ and $I_{c2}(\lambda)^c$ representing the intensity of the first and second portions **228** and **230** of the return light **220** at different wavelengths can then be used to determine the attenuation coefficient $\alpha(\lambda)$ of the sample **214** as described below.

At column 10, lines 45-61, please amend the paragraph as follows:

A4 Whether the measured attenuation accounts for absorption and/or scattering is mainly determined by the wavelength band of interest and the nature of the sample. The optical properties of biological tissue and the effects of tissue on LIF are greatly different for the wavelengths below and above approximately 600 nm. Below about 600 nm, the optical attenuation of biological tissue is primarily due to absorption and, hence, the attenuation coefficient $\alpha(\lambda)$ will represent absorptivity

$[\alpha(\lambda)]$ a(λ). Absorptivity is a property of a substance, while absorbance is a property of a particular sample of a substance. Therefore, absorbance will vary with the concentration of the substance (e.g., hemoglobin) and geometry of the tip of the probe. Thus, for samples such as biological tissue where the attenuation of the sample is primarily due to absorption, the absorbance $A(\lambda)$ and the percent transmittance $\%T(\lambda)$ of the sample can be calculated as follows:

At column 13, line 10, please amend equation (10) as follows:

$$\alpha(\lambda) = \{1/y^3\} \ln\{I_{[cx]xc}(\lambda)^c/I_{co}(\lambda)^c\}$$

At column 13, lines 29 - 37, please amend the paragraph as follows:

As discussed in connection with the previous embodiment, the measured attenuation may account for absorption and/or scattering depending on the wavelength band of interest and the nature of the sample. Below about 600 nm, the optical attenuation of biological tissue is primarily due to absorption and, hence, the attenuation coefficient $\alpha(\lambda)$ will represent absorptivity $[\alpha(\lambda)]$ a(λ). Also, the absorbance $A(\lambda)$ and the percent transmittance $\%T(\lambda)$ of such samples can be calculated as follows:

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At column 16, line 49, through column 17, line 7, please amend the paragraph as follows:

FIG. **9** shows three alternative geometrical configurations of the collection-only optical fibers **[950]450'***a-h* about the excitation-collection waveguide **[946]446'**. In these embodiments, it is desirable to couple each of the collection-only waveguides **[950]450'***a-h* to a separate sensor so that the intensity of each portion of the return light collected by each fiber can be monitored. In FIG. **9**(*a*), the collection-only waveguides **[950]450'***a-h* are arranged about the excitation-collection waveguide **[946]446'** so that their apertures have a helical configuration.

Because the aperture of each successive collection-only waveguide is shifted axially away from the aperture **[947]**447' of the excitation-collection waveguide **[946]**446', the return light collected by each of the collection-only waveguides **[950]**450'*a-h* will be attenuated in varying degrees. Use of a probe arrangement having a plurality of collection distances will be useful in measuring the polarization and/or the attenuation of, especially, a sample having a higher sensitivity to attenuation due to absorption. Furthermore, a probe incorporating a plurality of collection distances [have] has application to a larger variety of samples. For example, where the sample is highly attenuating, the collection-only waveguides having apertures close to the excitation site can be used to collect the return light. Where the sample is lightly attenuating, the return light collected by the waveguides having apertures that are further from the excitation site will be useful in determining the attenuation.

A8 (concluded)

At column 17, lines 8-18, please amend the paragraph as follows:

In FIG. **9**(*b*), the collection-only waveguides **[950]**450'*a-c* are displaced laterally with respect to the excitation-collection waveguide **[946]**446'. Such a probe configuration will be useful in measuring the polarization and/or the attenuation of the sample where the sample has a higher sensitivity to attenuation due to scattering. The return light collected by the waveguide **[950]**450'*c* will be useful in measuring attenuation of a lightly attenuating sample. On the other hand, the return light measured by the closest waveguide **[950]**450'*a* will be useful in measuring the attenuation of a heavily-attenuating sample.

A9

At column 17, lines 19-23, please amend the paragraph as follows:

In FIG. **9**(*c*), the collection-only waveguides **[950]**450'*a-c* are both axially and laterally displaced with respect to the excitation-collection waveguide **[946]**446'. This configuration combines the advantages of both of the aforementioned configurations shown in FIGS. **9**(*a*) and **9**(*b*).

A10

At column 18, lines 30-57, please amend the paragraph as follows:

--Another parameter found to be useful in the classification of normal, ischemic and hypoxic tissue, is the intensity of return light from a pair of LIFAS collection pathways (i.e., $[I_{c1}(\lambda)^c, I_{c2}(\lambda)^c]$ or $[I_{xc}(\lambda)^c, I_{co}(\lambda)^c]$ for the LIFAS embodiments described above[.]). For example, FIG. **13** shows the $[I_{xc}(\lambda)^c, I_{co}(\lambda)^c]$ pair at λ=480 nm, symbolized as $[I_{xc}(480)^c, I_{co}(480)^c]$, measured from hyper-oxygenated (x), normal (o) and oxygen deficient (+) rabbit kidney. The $[I_{xc}(480)^c, I_{co}(480)^c]$ from normal and oxygen-deficient tissue tend to cluster in two linearly separable regions of the two dimensional $I_{xc}(\lambda)^c$-$I_{co}(\lambda)^c$ space. Thus, a simple linear or nonlinear classifier function can be trained on a set of $[I_{xc}(\lambda)^c[c], I_{co}(\lambda)^c]$ pairs measured using a LIFAS system from normal, ischemic and hypoxic tissue. Other classifiers such as artificial neural networks (ANN) are also being used. The trained classifier function can then be used to classify an unknown $[I_{xc}(\lambda)^c, I_{co}(\lambda)^c[\,]]$ pair as normal, ischemic or hypoxic. A "nearest neighbor" (NN) classifier has been found to perform satisfactorily. The NN classifier checks the proximity of an unknown $[I_{xc}(480)^c, I_{co}(480)^c]$ pair to clusters of predetermined $[I_{xc}(480)^c, I_{co}(480)^c]$ pairs measured from known normal, ischemic and hypoxic tissue. Other classifiers such as artificial neural networks (ANN) can also be utilized. For myocardial and renal tissue it has been found that it is preferable to use $[I_{xc}(\lambda)^c, I_{co}(\lambda[^c])^c]$ measured at 480 nm, to optimize signal-to-noise ratio. However, $[I_{xc}(\lambda)^c, I_{co}(\lambda)^c]$ at other single or multiple pre-selected wavelengths can also be used.--

A11

At column 18, line 58 through column 19, line 15, please amend the paragraph as follows:

--An additional parameter for the classification of normal, ischemic and hypoxic tissue, is the wavelength of the peak transmittance of the tissue, symbolized hereafter as $\lambda_{max\text{-}T}$, especially in the 450-500 nm band. An alternative to $\lambda_{max\text{-}T}$ is the wavelength of the peak $I_{co}(\lambda)^c$ in the 450-500 nm band, symbolized hereafter as $\lambda_{max\text{-}co}$. Both $\lambda_{max\text{-}T}$ and $\lambda_{max\text{-}co}$ shift towards

A12

shorter wavelengths as the hemoglobin in the tissue becomes deoxygenated. For example, FIG. **14** shows $I_{co}(\lambda)^c$ spectra that are acquired using the LIFAS system shown in FIG. **10** employing 308 nm excitation radiation produced by an[d] XeCl excimer laser. It should be noted that the $\lambda_{max\text{-}co}$ of normal tissue shifts to a shorter wavelength as the tissue becomes hypoxic; whereas the $\lambda_{max\text{-}co}$ of normal tissue shifts to a longer wavelength as the tissue becomes hyperoxic. Specifically, $\lambda_{max\text{-}co}$ varies between about 480 and 500 nm as blood or hemoglobin oxygenation varies between deoxygenated to oxygenated, respectively. A separation border can be identified at about 489.5 nm to separate $\lambda_{max\text{-}co}$ of normal tissue (peaks above 489.5 nm) from hypoxic/ischemic tissue (peaks below 489.5 nm). A simple classifier can be trained to identify tissue as hypoxic if its $\lambda_{max\text{-}co}$ is below 489.5, and vice versa. The degree of hypoxia is determined from the magnitude of the shift in $\lambda_{max\text{-}co}$ from the normal value, the smaller the shift, the subtler the hypoxia.

A12 (concluded)

In the Claims:

1.(Amended) A spectroscopic method of analyzing a sample, comprising:

A13

irradiating a sample with radiation to produce fluorescence from the sample, wherein the fluorescence is modulated by the sample;

monitoring a first portion of the modulated fluorescence at a first distance from the sample;

monitoring a second portion of the modulated fluorescence at a second distance from the sample, the second distance being different from the first distance; and

comparing the first and second portions of the modulated fluorescence to each other to determine a modulation characteristic of the sample.

A14

20.(Amended) The method of claim [11] 1, wherein the method further includes determining the intrinsic fluorescence of the sample.